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(54) Title: CARBAZOLE DERIVATIVES AND THEIR USE FOR THE PREPARATION OF PHARMACEUTICAL COMPOSITIONS FOR THE TREATMENT OF NPY RELATED DISEASES

(57) Abstract: The invention relates to novel carbazole derivatives, their use for the preparation of a pharmaceutical composition for the treatment of eating and metabolic disorders such as obesity, bulimia nervosa, anorexia nervosa, of sleep disturbance, of morphine withdrawal symptoms and of epileptic seizures, a pharmaceutical composition containing them and a process for preparing them.

Carbazole derivatives and their use for the preparation of pharmaceutical compositions for the treatment of NPY related diseases

The invention relates to novel carbazole derivatives and their use for the preparation of pharmaceutical compositions for the treatment of eating and metabolic disorders such as obesity, bulimia nervosa, anorexia nervosa, of sleep disturbance, of morphine withdrawal and of epileptic seizures.

Background of the invention

Neuropeptide Y (NPY) is a 36 amino acid peptide discovered by Tatemoto in 1982 (Tatemoto, K. et al., Neuropeptide Y: complete amino acid sequence of the brain peptide. Proc. Natl. Acad. Sci. U.S.A. (1982), 79(18), 5485-9). Since its discovery, NPY has been found in the brain in concentrations higher than any other putative neurotransmitter. Hypothalamic regions are particularly rich in NPY-containing neurons, with the paraventricular nucleus containing perhaps the highest concentration of NPY in the brain.

Evidence suggests the existence of several NPY receptor subtypes among which hY1 (Larhammar et al., Cloning and functional expression of a human neuropeptide Y/peptide YY receptor of the Y1 type. J. Biol. Chem., 1992, 267(16), 10935-8.), hY2 (WO 95/21245), hY4 (WO 95/17906), hY5 (Gerald et al., Cloning and expression of a novel neuropeptide Y receptor. J. Biol. Chem. 271, 16435, 1996.; WO97/46250) and hY6 have been cloned (hY6: Weinberg et al., Cloning and expression of a novel neuropeptide Y receptor. J. Biol. Chem., 1996), 271(28), 16435-8). However, the Y6 receptor appears to be nonfunctional in humans. The NPY receptor subclassification is based mainly on the activity/affinity profile of NPY/PYY/PP and certain selective analogs/fragments (Michel M.C., et al., XVI. International Union of Pharmacology recommendations for the nomenclature of neuropeptide Y, peptide YY, and pancreatic polypeptide receptors. Pharmacol. Rev. 1998 Mar; 50(1):143-50).

NPY is the most potent stimulant of food intake. Chronic i.c.v. administration of NPY in rats results in a robust increase in food intake associated with an increase in body weight and body fat content (White, Neuropeptide Y: a central regulator of energy homeostasis. Regul. Pept. 1993, 49(2), 93-107). Because NPY does not only increase food intake but also reduces energy expenditure it has been hypothesized that NPY could be an important brain peptide regulating energy balance. Moreover, food deprivation in rats is associated with an increase in NPY concentrations in the

hypothalamus (Frankish et al., Neuropeptide Y, the hypothalamus, and diabetes: Insights into the central control of metabolism. Peptides, 16, 4, 757 – 771, 1995). This fluctuation of NPY levels in the brain with different feeding states supports a physiological role for NPY in feeding. Antisera against NPY (Dube M.G. et al., Evidence that neuropeptide Y is a physiological signal for normal food intake. Brain Res. (1994), 646(2), 341-4) as well as peptide (Myers et al, Anorexic action of a new potential neuropeptide Y antagonist [D-Tyr27,36,D-Thr32]-NPY (27-36) infused into the hypothalamus of the rat. Brain Res. Bull. 1995, 37(3), 237-45) and nonpeptide antagonists attenuate the hyperphagia seen after food deprivation. In addition, hypothalamic concentrations of NPY as well as NPY mRNA, are increased in genetically obese animals, such as the fatty Zucker rat or the ob/ob mouse (Frankish et al., Neuropeptide Y, the hypothalamus, and diabetes: Insights into the central control of metabolism. Peptides, 16, 4, 757 – 771, 1995).

Accordingly, NPY antagonists seem to be promising candidates for the treatment of obesity. The characterization of the NPY receptor subtype responsible for food intake in rats is mainly based on functional experiments. The agonist receptor binding profile suggests that the Y5 receptor is involved in the NPY induced feeding behavior. Thus Y5 antagonists inhibit NPY mediated feeding as well as food intake in 24 hours food deprived rats (Criscione, L. et al., Food intake in free-feeding and energy-deprived lean rats is mediated by the neuropeptide Y5 receptor. J. Clin. Invest.1998, 102(12), 2136-2145; Kask et al. Neuropeptide Y Y5 receptor antagonist CGP71683A: the effects on food intake and anxiety-related behavior in the rat. Eur. J. Pharmacol., 2001, 414(2/3), 215-224) supporting the notion that the Y5 receptor is the "feeding" receptor. In addition, Hwa J.J. et al. (Activation of the NPY Y5 receptor regulates both feeding and energy expenditure. Am J Physiol 277(5 Pt 2), R1428-R1434, 1999) demonstrated a reduced oxygen consumption and energy expenditure in rats upon administration of a Y5 agonist, thereby further substantiating the role of the Y5 receptor in energy homeostasis. However, Y1 selective antagonists such as BIBO3304 and 1229U91 inhibit the NPY induced feeding in rodents and in primates (rhesus monkey experiments using 1229U91) too.

Other fields for the use of NPY Y5 receptor ligands have been demonstrated for the treatment of morphine withdrawal (Woldbye D.P.et al., Neuropeptide Y attenuates naloxone-precipitated morphine withdrawal via Y5-like receptors. J Pharmacol Exp Ther 284(2), 633-636, 1998), based on the attenuation of these effect upon i.c.v. administration of Y5 selective agonists, and for seizures, based on the reduced exhibition of spontaneous seizures in Y5 knock out mice (Marsh D.J. et al., Role of

the Y5 neuropeptide Y receptor in limbic seizures. Proc Natl Acad Sci USA 96(23), 13518-13523, 1999) as well as administration of Y5 selective agonists (Woldbye D.P. et al., Powerful inhibition of kainic acid seizures by neuropeptide Y via Y5-like receptors. Nature Medicine, 1997, 3(7), 761-4) in seizure models. Influence of the Y5 receptors in the hypothalamic suprachiasmatic nucleus on the circadian rhythm have been reported by Gribkoff V. K. et al (Phase shifting of circadian rhythms and depression of neuronal activity in the rat suprachiasmatic nucleus by neuropeptide Y: mediation by different receptor subtypes. J Neurosci. 18(8), 3014-3022, 1998).

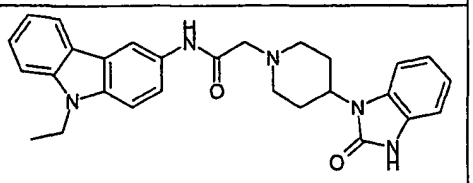
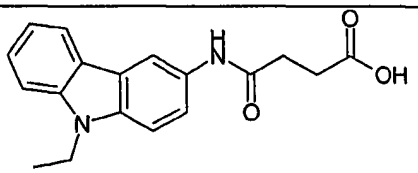
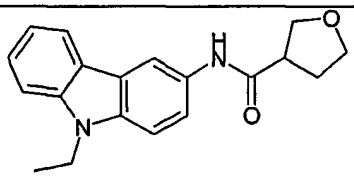
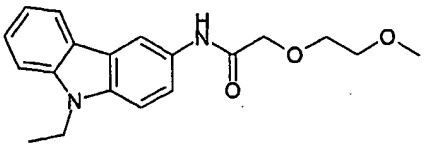
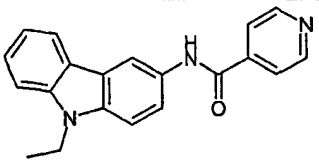
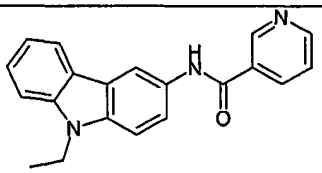
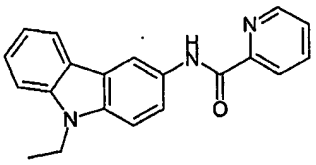
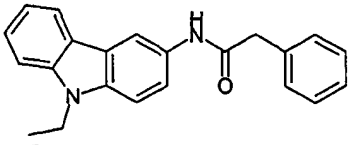
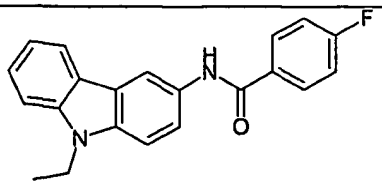
Summary of the invention

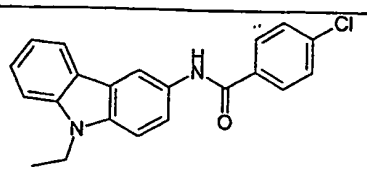
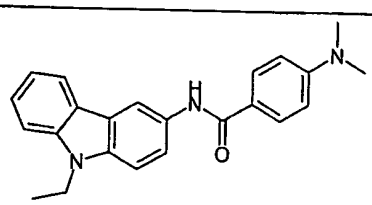
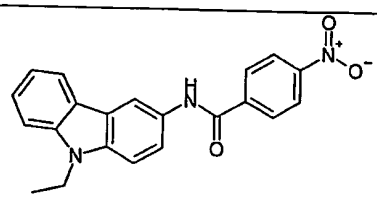
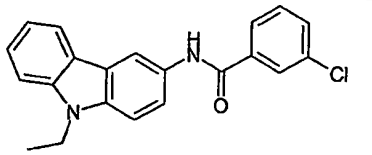
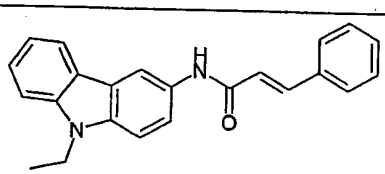
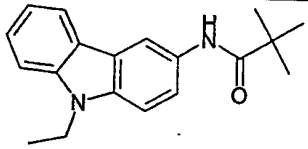
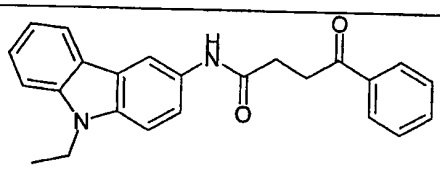
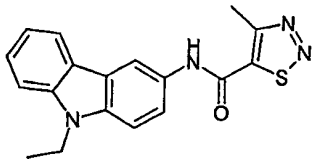
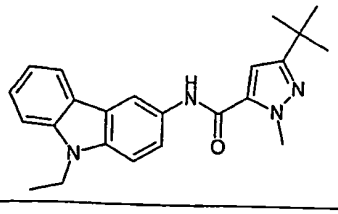
This invention is directed to novel carbazole compounds which bind selectively to and modulate, i.e. inhibit or stimulate, the activity of the human Y5 receptor. The invention relates to new compounds as listed in Table 1, or a salt thereof, to pharmaceutical compositions containing them, and to the manufacture of new compounds as listed in Table 1 and salts thereof. The invention furthermore relates to a method of treatment of disorders and diseases associated with NPY receptor subtype Y5, such as eating and metabolic disorders, of sleep disturbance, of morphine withdrawal and of epileptic seizures and to the use of the compounds according to the invention for the preparation of a pharmaceutical composition for treating said disorders and diseases.

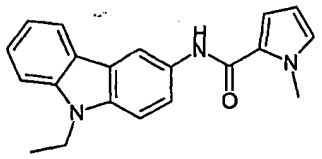
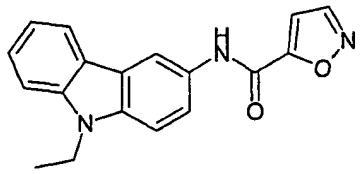
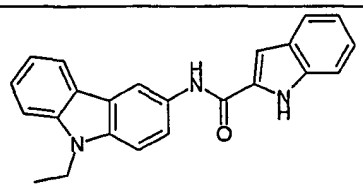
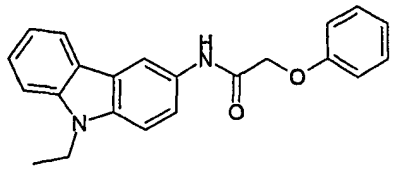
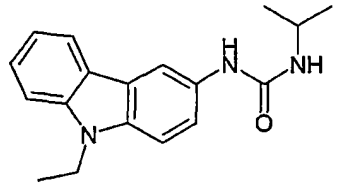
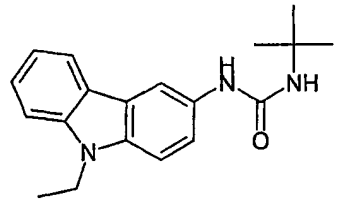
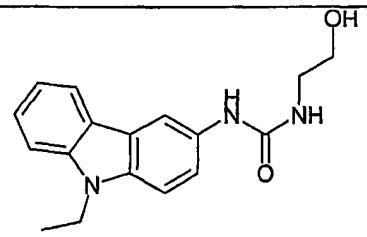
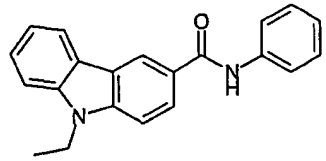
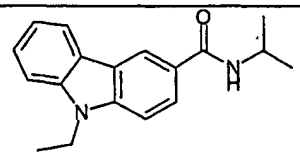
Detailed description of the invention

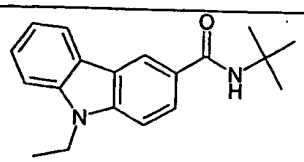
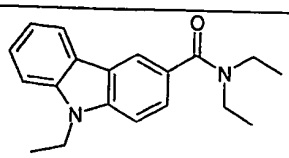
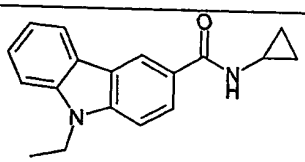
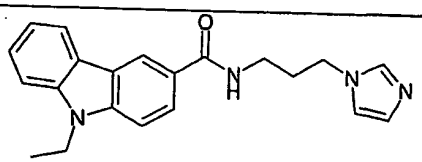
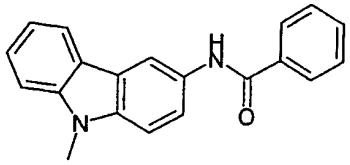
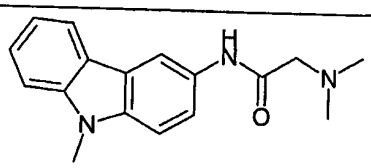
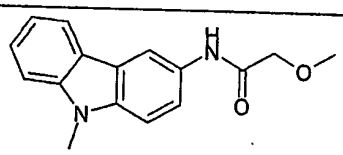
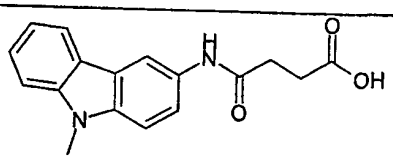
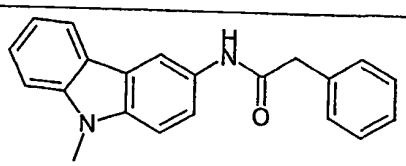
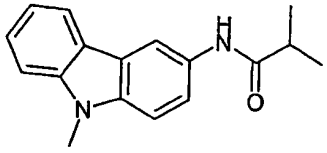
It has now been found that the new compounds as listed in Table 1 and the diastereomers, enantiomers, mixtures and salts thereof, and in particular the physiologically acceptable salts thereof, are useful for the treatment of eating and metabolic disorders such as obesity, bulimia nervosa, anorexia nervosa, of sleep disturbance, of morphine withdrawal symptoms and of epileptic seizures.

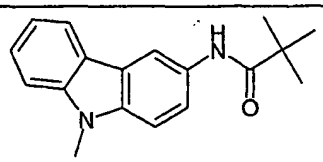
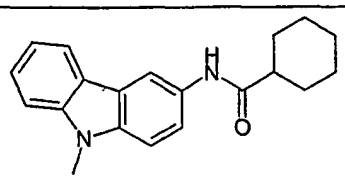
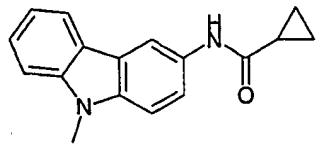
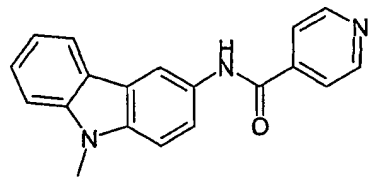
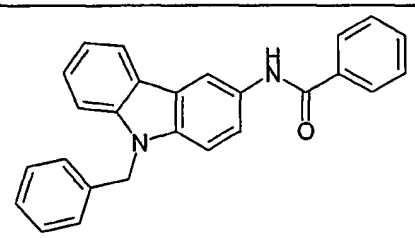
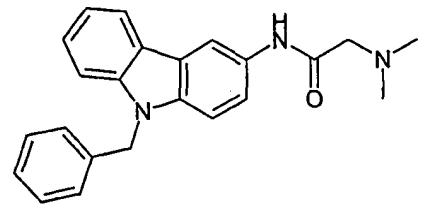
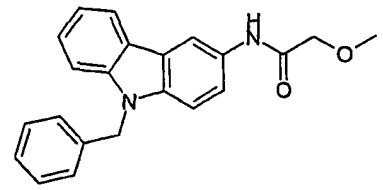
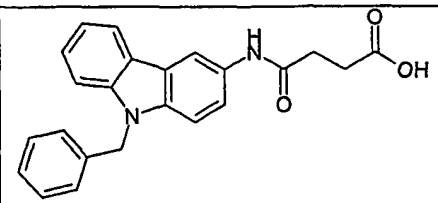
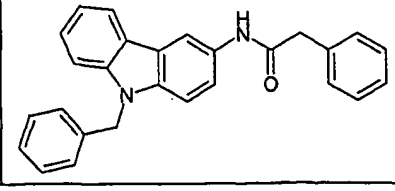
Table 1: New compounds useful for the treatment of NPY related diseases

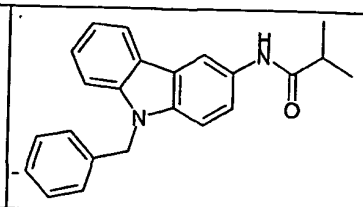
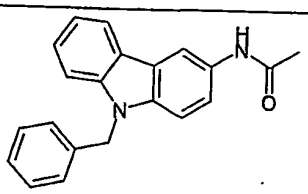
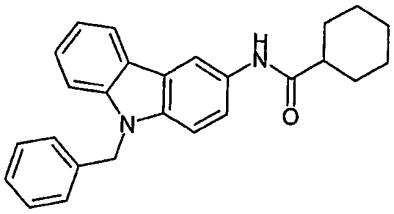
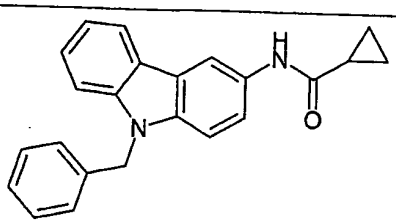
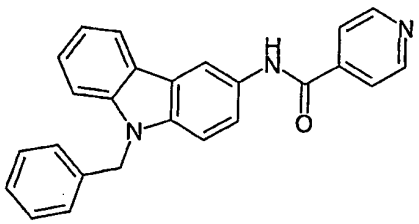
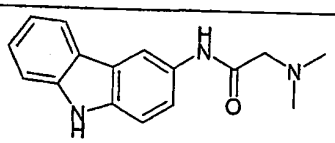
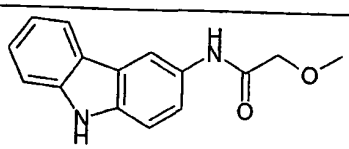
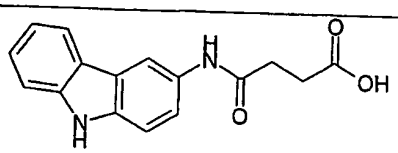
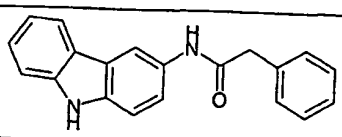
No.	Chemical name	Chemical formula
26-1	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	
26-2	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-succinamic acid	
26-3	Tetrahydro-furan-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-4	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-(2-methoxy-ethoxy)-acetamide	
26-5	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-isonicotin-amide	
26-6	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-nicotinamide	
26-7	Pyridine-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-8	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	
26-9	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-fluoro-benzamide	

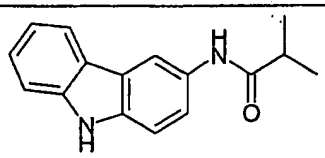
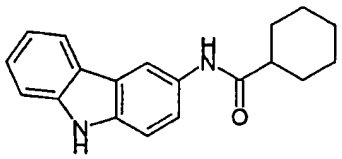
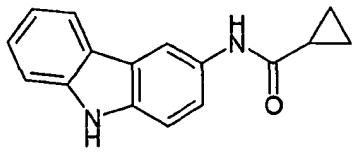
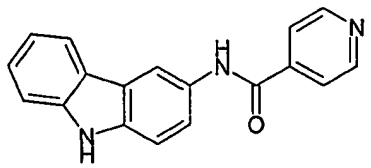
26-10	4-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-12	4-Dimethylamino-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-13	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-nitro-benzamide	
26-14	3-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-15	(E)-*N*-(9-Ethyl-9*H*-carbazol-3-yl)-3-phenyl-acrylamide	
26-16	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2,2-dimethyl-propionamide	
26-17	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-oxo-4-phenyl-butyramide	
26-19	4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-20	5-*tert*-Butyl-2-methyl-2*H*-pyrazole-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	

26-21	1-Methyl-1*H*-pyrrole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-22	Isoxazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-24	1*H*-Indole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-25	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenoxy-acetamide	
27-1	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-isopropyl-urea	
27-2	1-*tert*-Butyl-3-(9-ethyl-9*H*-carbazol-3-yl)-urea	
27-3	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-(2-hydroxy-ethyl)-urea	
28-1	9-Ethyl-9*H*-carbazole-3-carboxylic acid phenylamide	
28-2	9-Ethyl-9*H*-carbazole-3-carboxylic acid isopropylamide	

28-3	9-Ethyl-9*H*-carbazole-3-carboxylic acid *tert*-butylamide	
28-4	9-Ethyl-9*H*-carbazole-3-carboxylic acid di-ethylamide	
28-5	9-Ethyl-9*H*-carbazole-3-carboxylic acid cyclopropylamide	
28-6	9-Ethyl-9*H*-carbazole-3-carboxylic acid (3-imidazol-1-yl-propyl)-amide	
29-1	*N*-(9-Methyl-9*H*-carbazol-3-yl)-benzamide	
29-2	2-Dimethylamino-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
29-3	2-Methoxy-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
29-4	*N*-(9-Methyl-9*H*-carbazol-3-yl)-succinamic acid	
29-5	*N*-(9-Methyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	
29-6	*N*-(9-Methyl-9*H*-carbazol-3-yl)-isobutyramide	

29-7	2,2-Dimethyl-*N*-(9-methyl-9*H*-carbazol-3-yl)-propionamide	
29-8	Cyclohexanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
29-9	Cyclopropanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
29-10	*N*-(9-Methyl-9*H*-carbazol-3-yl)-isonicotinamide	
30-1	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-benzamide	
30-2	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-dimethylamino-acetamide	
30-3	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-methoxy-acetamide	
30-4	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-succinamic acid	
30-5	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	

30-6	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isobutyr-amide	
30-7	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-acetamide	
30-8	Cyclohexanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
30-9	Cyclopropanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
30-10	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isonicotin-amide	
31-1	*N*-(9*H*-Carbazol-3-yl)-2-dimethylamino-acetamide	
31-2	*N*-(9*H*-Carbazol-3-yl)-2-methoxy-acetamide	
31-3	*N*-(9*H*-Carbazol-3-yl)-succinamic acid	
31-4	*N*-(9*H*-Carbazol-3-yl)-2-phenyl-acetamide	

31-5	N-(9*H*-Carbazol-3-yl)-isobutyramide	
31-6	Cyclohexanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
31-7	Cyclopropanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
31-8	*N*-(9*H*-Carbazol-3-yl)-isonicotinamide	

The present invention relates to the new compounds mentioned above, the diastereomers, enantiomers, mixtures and salts thereof, particularly to the pharmaceutically acceptable salts thereof, to their use for the treatment of eating and metabolic disorders such as obesity, bulimia nervosa, anorexia nervosa, of sleep disturbance, of morphine withdrawal symptoms and of epileptic seizures, to their use for the preparation of apharmaceutical composition for treating said disorders and diseases, pharmaceutical compositions containing them and processes for preparing them.

Preferred compounds are:

(a) tetrahydro-furan-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide
(b) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2-(2-methoxy-ethoxy)-acetamide
(c) *N*-(9-ethyl-9*H*-carbazol-3-yl)-nicotinamide
(d) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide
(e) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2,2-dimethyl-propionamide
(f) *N*-(9-ethyl-9*H*-carbazol-3-yl)-4-oxo-4-phenyl-butyramide
(g) 2-chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide
(h) 1-(9-ethyl-9*H*-carbazol-3-yl)-3-isopropyl-urea
(i) 1-(9-ethyl-9*H*-carbazol-3-yl)-3-(2-hydroxy-ethyl)-urea
(j) *N*-(9-methyl-9*H*-carbazol-3-yl)-isobutyramide
(k) 2,2-dimethyl-*N*-(9-methyl-9*H*-carbazol-3-yl)-propionamide
(l) cyclopropanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide

and the diastereomers, enantiomers, mixtures and salts thereof, particularly to the pharmaceutically acceptable salts thereof.

The compounds according to the invention, if they contain a basic group, may be converted into their salts, particularly, for pharmaceutical use, into their physiologically acceptable salts, with inorganic or organic acids. Suitable acids for this purpose include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, fumaric acid, succinic acid, lactic acid, citric acid, tartaric acid or maleic acid.

Furthermore, the compounds according to the invention, if they contain a carboxy group, may, if desired, be converted subsequently into their salts with inorganic or organic bases, particularly, for pharmaceutical use, into their physiologically acceptable salts. Examples for suitable bases include sodium hydroxide, potassium hydroxide, cyclohexylamine, ethanolamine, diethanolamine and triethanolamine.

As already mentioned hereinbefore, the new compounds as listed in Table 1 and the salts thereof have valuable pharmacological properties and are useful for the treatment of eating and metabolic disorders such as obesity, bulimia nervosa, anorexia nervosa, of morphine withdrawal symptoms, of epileptic seizures or of sleep disturbance, particularly for the treatment of obesity.

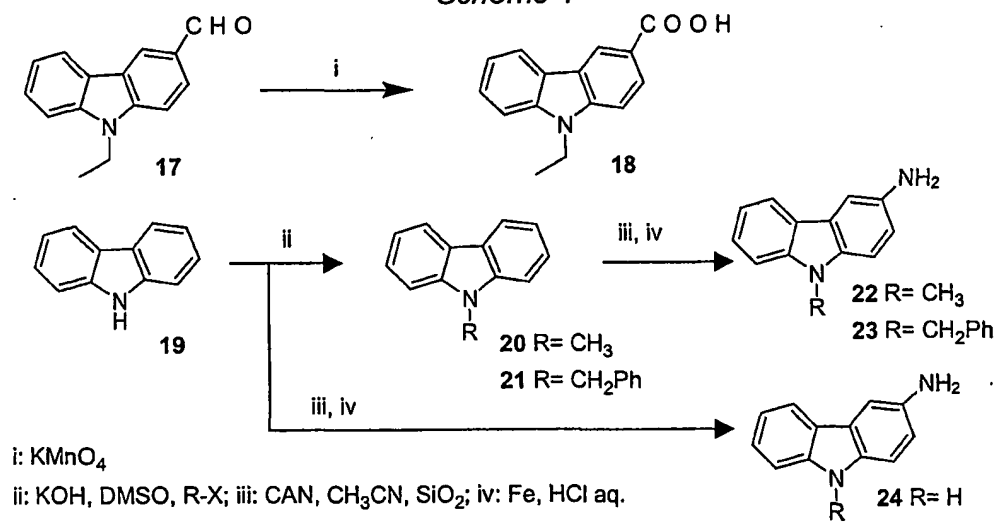
In the synthetic section, the following abbreviations are used:

Ac	acetyl
aq.	aqueous
DMSO	dimethylsulfoxide
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimid
Hünig´s base	ethyl-diisopropyl-amine
min.	minutes
org.	organic
PyCloP	chlorotripyrrolidinophosphonium hexafluorophosphate
sat.	saturated
CAN	ceric ammonium nitrate
SiO_2	silica

Synthetic methods

The syntheses of the key building blocks 18 and 22 to 24 are described in *Scheme 1*. Carbazol 25 was commercially available from Aldrich.

Scheme 1



Procedure for the synthesis of acid 18:

To a stirred solution of 5.0 g Na_2CO_3 and 15.0 g $KMnO_4$ in water (250 ml) was added 5.0 g (22.4 mmol) 9-ethyl-3-carbazole carboxaldehyde. The reaction mixture was refluxed for 5 h, then allowed to cool to room temperature and treated with 10% aq. NaH_2PO_4-solution until pH 6 was reached. The reaction mixture was extracted with EtOAc, the org. layer washed with sat. Brine, dried ($MgSO_4$), evaporated and the residue dried under reduced pressure to yield 3.6 g of crude product, which after re-crystallization from EtOAc gave 1.49 g (27.8%) of acid 18.

1H-NMR (300 MHz, DMSO-d_6): 12.60 (br. S, 1H); 8.80 (m, 1H); 8.26 (dd, J= 0.5, 7.2, 1H); 8.05 (dd, J=1.7, 8.7, 1H); 7.67-7.63 (m, 2H); 7.49 (dt, J= 1.1, 7.1, 1H); 4.47 (q, J=7.1, 2H); 1.31 (t, J= 7.1, 3H).

General procedures for the synthesis of carbazoles 22 to 24:

Alkylation:
Was performed according to *J. Chem. Soc. Perkin Trans I*, 1973, 499-500.

Nitration:
Was performed according to *Synthetic Commun.* 1994, *24*, 1-10.

Reduction of the nitro group:

A mixture of 32% aq. HCl-solution (24 ml) and EtOH (24 ml) was added dropwise to a mixture of the corresponding 3-nitro-carbazole (11.3 mmol) and iron powder (6.31 g, 113 mmol) in EtOH (48 ml). The reaction mixture was stirred for 90 min. at 80°C, cooled and poured onto a mixture of 2N NaOH-solution (350 ml) and ice. The mixture was extracted with EtOAc, the org. layer washed with 2N aq. NaOH-solution and sat. Brine, dried (Na_2SO_4) and evaporated. The crude residue was suspended in Et_2O, filtered and dried under reduced pressure.
Yields: 22 (93.7%); 23 (83%); 24 (67.1%).

22: 1H-NMR (300MHz, DMSO-d_6): 9.91 (m, 1H); 7.44-7.25 (m, 4H); 7.05 (ddd, J= 1.1, 6.9, 7.9, 1H); 6.81 (dd, J=2.0, 8.6, 1H); 4.71 (s, 2H); 3.74 (s, 3H).
23: 1H-NMR (300 MHz, DMSO-d_6): 7.95 (br. D, J= 7.7, 1H); 7.47 (d, J= 8.2, 1H), 7.33-7.04 (m, 9H); 6.77 (m (dd), 1H); 5.51 (s, 2H); 4.73 (s, 2H).
24: 1H-NMR (300 MHz, DMSO-d_6): 10.67 (br. S, 1H); 7.87 (m, 1H); 7.35-7.14 (m, 4H); 7.00 (ddd, J= 1.1, 6.8, 8.8, 1H); 6.74 (dd, J= 2.2, 8.4, 1H); 4.65 (br. S, 2H).

General procedure for the preparation of 26 and 29, 30 and 31:

From acid chlorides:

To a solution of 3-amino carbazoles 22 to 25 (0.25 mmol) in CH_2Cl_2 (1 ml) was added pyridine (1.25 mmol) and N,N-dimethylaminopyridine (0.05 mmol) and the corresponding acid chloride (0.3 mmol). The reaction mixture was stirred for 2-24 h at room temperature, evaporated to dryness and the residue was chromatographed on SiO_2 using hexane/EtOAc.

From carboxylic acids:

To a solution of 3-amino carbazoles 22 to 25 (0.25 mmol) in CH_2Cl_2 (1 ml) was added the corresponding carboxylic acid (0.38 mmol) and EDCI (0.38 mmol) at room temperature. The reaction mixture was stirred for 24 h at room temperature and extracted with $NaHCO_3$-solution and EtOAc. The org. layer was dried ($MgSO_4$), evaporated and the residue chromatographed on SiO_2 as described above.

General procedure for the preparation of 27:

To 0.3 mmol of the corresponding amine or aniline in CH_3CN were added 0.11 mmol triphosgene and 0.9 mmol Hünig's base at 4°C to give a clear solution, which was stirred at room temperature (30 min.) and for 2 h at 75°C. The reaction mixture was cooled to room temperature followed by addition of 25 (0.25 mmol). The reaction mixture was heated for 3 h at 75°C, evaporated to dryness and the residue was chromatographed on SiO_2 with hexane/EtOAc.

General procedure for the preparation of 28:

To a mixture of acid 18 (0.25 mmol) and the corresponding aniline or amine (0.28 mmol) in CH_2Cl_2 (1 ml) was added chlorotripyrrolidinophosphonium hexafluorophosphate (PyCloP) (0.28 mmol) and Hünig's base (1.05 mmol). The reaction mixture was stirred for 15 h at room temperature, extracted with water and EtOAc, the org. layer was dried ($MgSO_4$), evaporated and the residue chromatographed on SiO_2 with hexane/EtOAc.

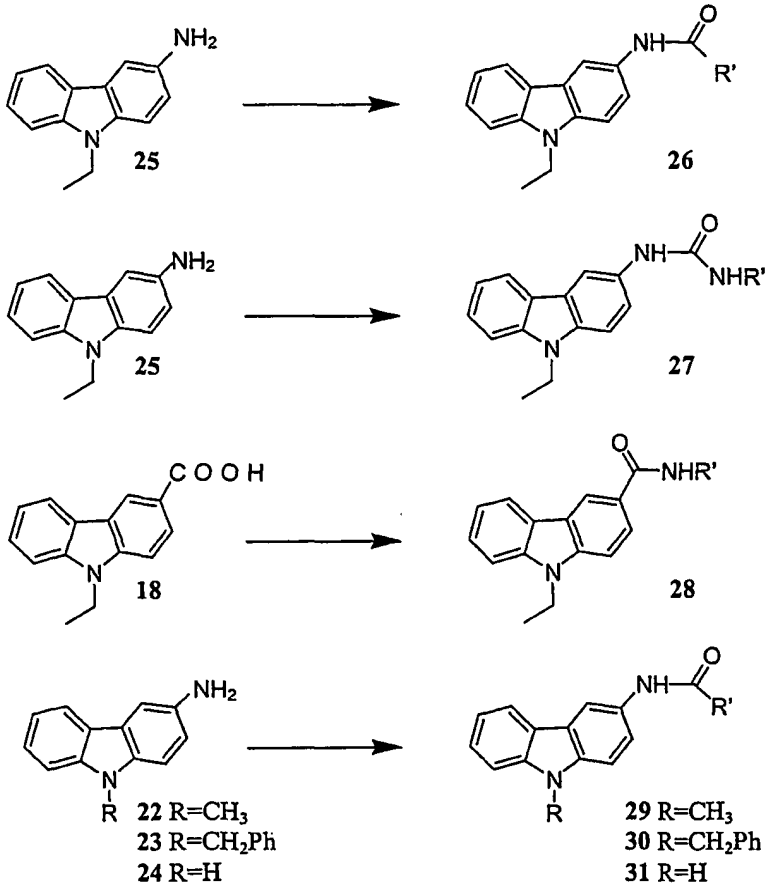
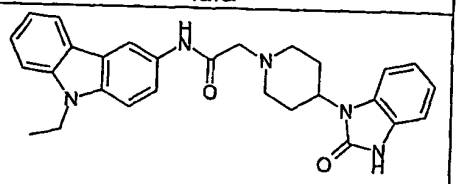
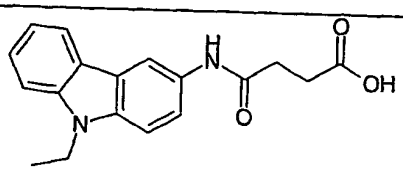
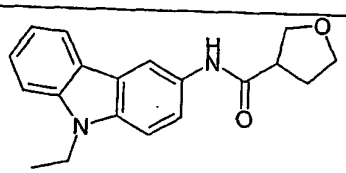
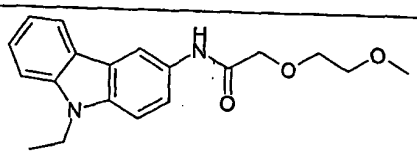
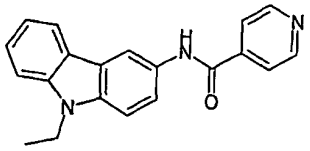
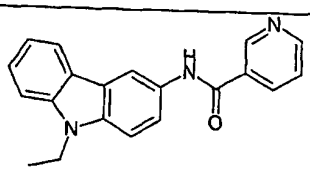
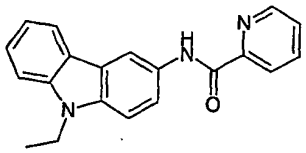
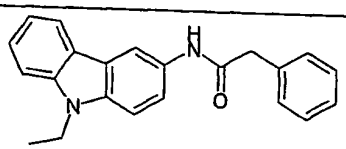
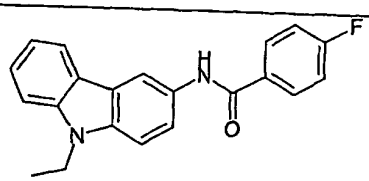
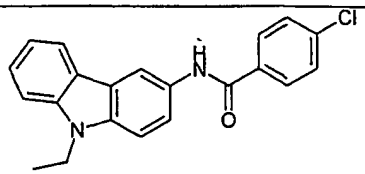
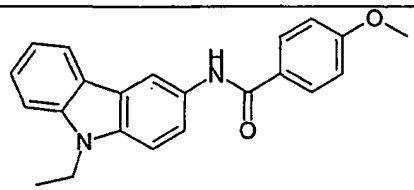
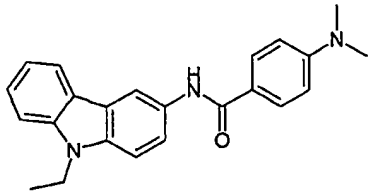
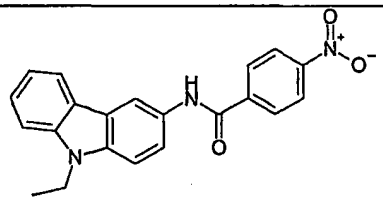
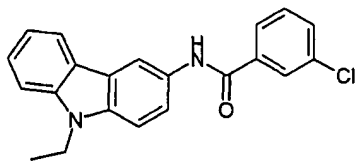
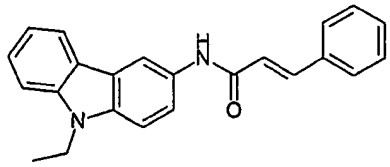
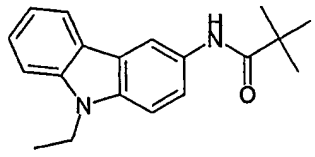
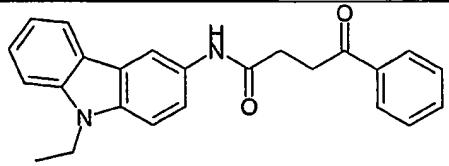
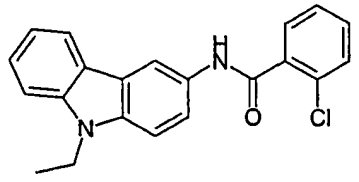


Table 2a: Examples for compounds of general formula 26:

No.	Chemical name	Chemical formula
Example 26-1	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	
Example 26-2	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-succinamic acid	
Example 26-3	Tetrahydro-furan-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-4	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-(2-methoxy-ethoxy)-acetamide	
Example 26-5	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-iso-nicotinamide	
Example 26-6	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-nicotinamide	
Example 26-7	Pyridine-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-8	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	
Example 26-9	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-fluoro-benzamide	

Example 26-10	4-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
Example 26-11	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-methoxy-benzamide	
Example 26-12	4-Dimethylamino-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
Example 26-13	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-nitro-benzamide	
Example 26-14	3-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
Example 26-15	(E)-*N*-(9-Ethyl-9*H*-carbazol-3-yl)-3-phenyl-acrylamide	
Example 26-16	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2,2-dimethyl-propionamide	
Example 26-17	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-oxo-4-phenyl-butyramide	
Example 26-18	2-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	

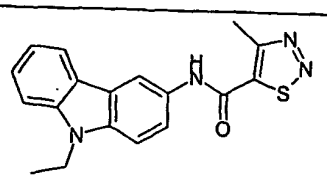
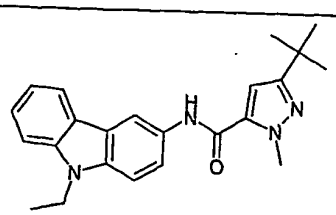
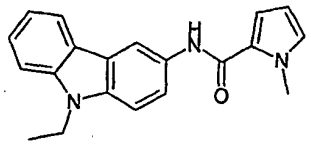
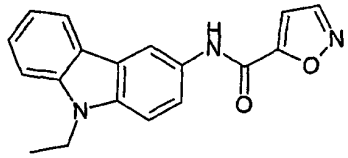
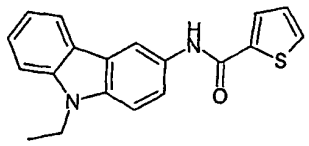
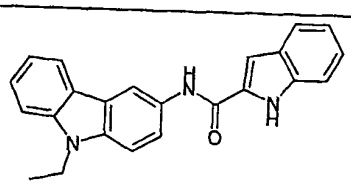
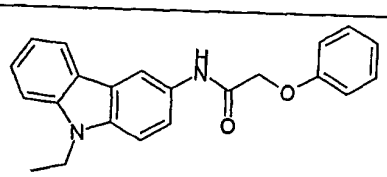
Example 26-19	4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-20	5-*tert*-Butyl-2-methyl-2*H*-pyrazole-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-21	1-Methyl-1*H*-pyrrole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-22	Isoxazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-23	Thiophene-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-24	1*H*-Indole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
Example 26-25	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenoxy-acetamide	

Table 2b: Experimental data of the compounds listed in table 2a

	1H NMR (300MHz)		Mass Spectrum		
	Solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 26-1			467,5756	468.5	466.5
Example 26-2	DMSO-d_6	1.28 (t, 3H); 2.55 (2t, 4H); 4.39 (q, 2H); 7.12 (t, 1H); 7.41 (t, 1H); 7.52 (m, 3H); 8.01 (d, 1H); 8,40 (s, 1H); 9.98 (s, 1H); 12.3 (s, 1H)	310,3558	311.6	309.2
Example 26-3			308,3835	309.2	307.5

Example 26-4	DMSO-d_6	1.28 (t, 3H); 3.30 (s, 3H); 3.45 (q, 2H); 3.68 (q, 2H); 4.09 (s, 2H); 4.40 (q, 2H); 7.16 (t, 1H); 7.42 (t, 1H); 7.68 (m, 3H); 8.04 (d, 1H); 8.40 (d, 1H); 9.60 (s, 1H)	326,3988	327.4	325.6
Example 26-5	DMSO-d_6	1.29 (t, 3H); 4.42 (q, 2H); 7.20 (t, 1H); 7.46 (t, 1H); 7.62 (t, 2H); 7.79 (dd, 1H); 8.07 (d, 1H); 8.30 (m, 2H); 8.60 (s, 1H); 8.97 (m, 2H); 10.91 (s, 1H)	315,378	316.4	-
Example 26-6	DMSO-d_6	1.31 (t, 3H); 4.43 (q, 2H); 7.13 (t, 1H); 7.44 (t, 1H); 7.58 (m, 3H); 7.73 (dd, 1H); 8.08 (d, 1H); 8.30 (dd, 1H); 8.52 (s, 1H); 8.74 (d, 1H); 9.16 (s, 1H); 10.48 (s, 1H)	315,378	316.3	-
Example 26-7	-		315,378	316.3	-
Example 26-8	-		328,4175	329.2	-
Example 26-9	DMSO-d_6	1.30 (t, 3H); 4.43 (q, 2H); 7.17 (t, 1 H); 7.30-7.46 (m, 3H); 7.58 (d, 2H); 8.08 (m, 3H); 8.31 (s, 1H); 10.30 (s, 1H)	332,3808	333.4	-
Example 26-10	DMSO-d_6	1.28 (t, 3H); 4.41 (q, 2H); 7.17 (t, 1H); 7.23 (t, 1H); 7.60 (m, 3H); 7.73 (d, 1H); 8.04 (m, 3H); 8.51 (s, 1H); 10.34 (s, 1H)	348,8354	349.2	-
Example 26-11	-		344,4169	345.2	343.4
Example 26-12	-		357,4593	358.4	-
Example 26-13	DMSO-d_6	1.30 (t, 3H); 4.44 (q, 2H); 7.18 (t, 1H); 7.44 (t, 1H); 7.60 (m, 2H); 7.75 (dd, 1H); 8.08 (d, 1H); 8.24 (d, 2H); 8.37 (d, 2H); 8.55 (s, 1H); 10.61 (s, 1H)	359,3879	360.5	-
Example 26-14	-		348,8354	349.3	348.3
Example 26-15	-		340,4287	341.2	-
Example 26-16	DMSO-d_6	1.2-1.3 (t+s; 12 H); 4.39 (q, 2H); 7.15 (t, 1H); 7.41 (t, 1H); 7.5-7.6 (m, 3H); 8.04 (d, 1H); 8.32 (d, 1H); 9.21 (s, 1H)	294,4	295.2	-
Example 26-17	-		370,4551	371.5	369.5
Example 26-18	-		348,8354	349.2	-
Example 26-19	-		336,4184	337.6	335.7
Example 26-20	-		374,4899	375.2	373.2
Example 26-21	-		317,3939	318.2	-
Example 26-22	-		305,3392	306.4	304.2
Example 26-23	DMSO-d_6	1.30 (t, 3H); 4.42 (q, 2H); 7.20 (m, 2H); 7.45 (t, 1H); 7.57 (d, 2H); 7.71 (dd, 1H); 7.83 (d, 1H); 8.05 (m, 2H); 1.45 (s, 1H); 10.38 (s, 1H)	320,4162	321.1	-
Example 26-24	-		353,4274	354.3	352.5
Example 26-25	-		344,4169	345.2	-

Table 3a: Examples for compounds of general formula 27

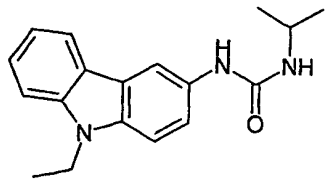
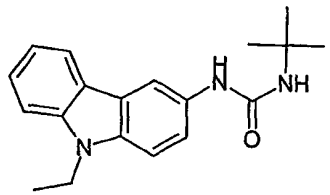
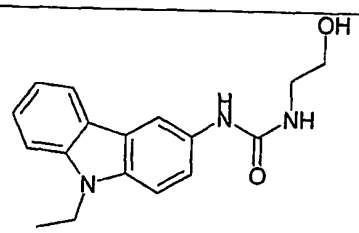
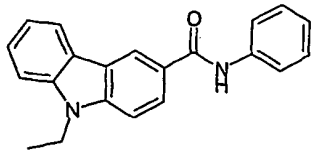
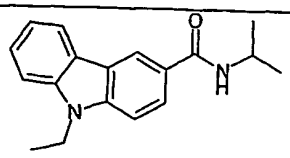
No.	Chemical name	Chemical formula
Example 27-1	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-isopropyl-urea	
Example 27-2	1-*tert*-Butyl-3-(9-ethyl-9*H*-carbazol-3-yl)-urea	
Example 27-3	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-(2-hydroxy-ethyl)-urea	

Table 3b: Experimental data of the compounds listed in table 3a

	1H NMR (300MHz)		Mass Spectrum		
	solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 27-1	-		295,3876	296.1	-
Example 27-2	-		309,4147	310.6	-
Example 27-3	DMSO-d_6	1.26 (t, 3H); 2.80 (t, 1H); 3.16 (q, 2H); 3.45 (m, 2H); 4.36 (q, 2H); 4.73 (m, 1H); 6.13 (t, 1H); 7.12 (t, 1H); 7.30- 7.54 (m, 5H); 8.01 (d, 1H); 8.15 (d, 1H); 8.47 (s, 1H)	297,3599	-	297.6

Table 4a: Examples for compounds of general formula 28

No.	Chemical name	Chemical formula
Example 28-1	9-Ethyl-9*H*-carbazole-3-carboxylic acid phenylamide	
Example 28-2	9-Ethyl-9*H*-carbazole-3-carboxylic acid isopropylamide	

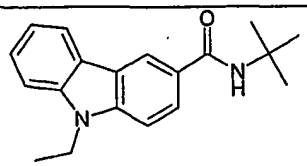
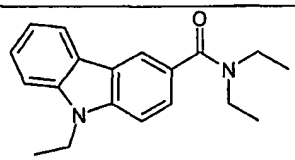
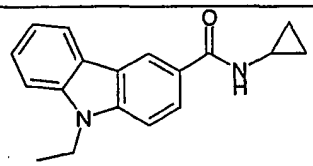
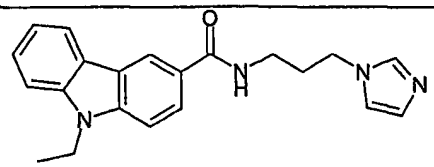
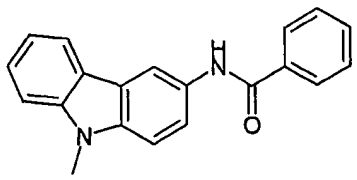
Example 28-3	9-Ethyl-9*H*-carbazole-3-carboxylic acid *tert*-butylamide	
Example 28-4	9-Ethyl-9*H*-carbazole-3-carboxylic acid diethylamide	
Example 28-5	9-Ethyl-9*H*-carbazole-3-carboxylic acid cyclopropylamide	
Example 28-6	9-Ethyl-9*H*-carbazole-3-carboxylic acid (3-imidazol-1-yl-propyl)-amide	

Table 4b: Experimental data of the compounds listed in table 4a

	1H NMR (300MHz)		Mass Spectrum		
	solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 28-1	-		314,3904	315.5	313.3
Example 28-2	-		280,3729	218.5	-
Example 28-3	-		294,4	295.5	-
Example 28-4	$CDCl_3$	1.23 (t, 6H); 1.40 (t, 3H); 3.49 (m, 4H); 4.37 (q, 2H); 7.20-7.60 (m, 4H); 8.08 (d, 1H); 8.16 (s, 1H)	294,4	295.4	-
Example 28-5	-		278,357	279.7	-
Example 28-6	$CDCl_3$	1.42 (t, 3H); 2.20 (p, 2H); 3.55 (q, 2H); 4.13 (t, 2H); 4.35 (q, 2H)6.71 (t, 1H); 7.07 (d, 2H); 7.20-7.55 (m, 4H); 7.90 (m, 2H); 8.15 (d, 1H); 8.55 (s, 1H)	346,436	347.4	345.1

Table 5a: Examples for compounds of general formula 29

No.	Chemical name	Chemical formula
Example 29-1	*N*-(9-Methyl-9*H*-carbazol-3-yl)-benzamide	

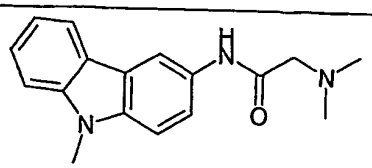
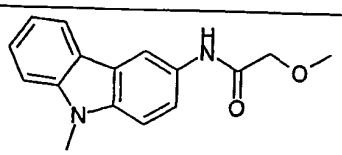
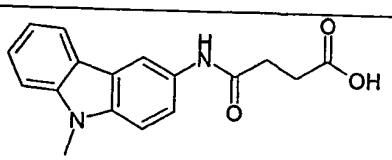
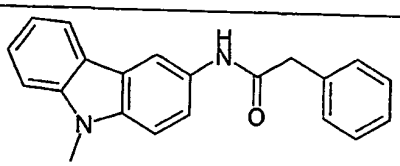
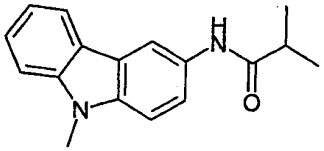
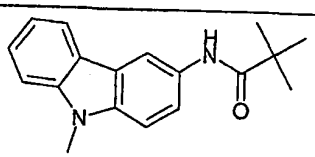
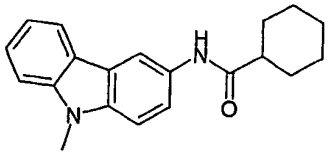
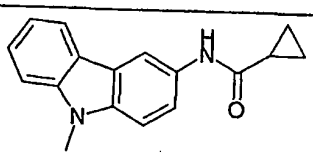
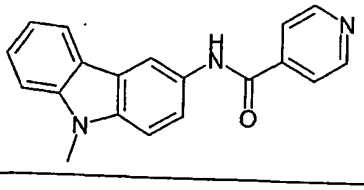
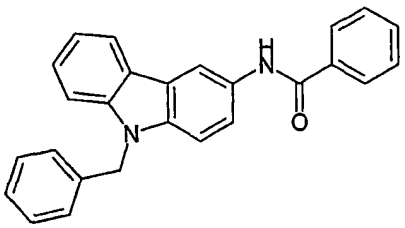
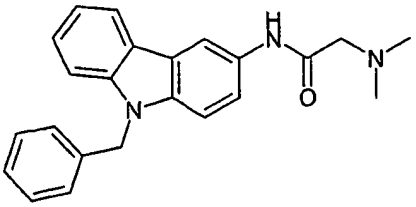
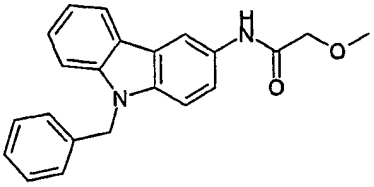
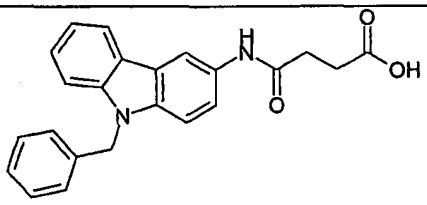
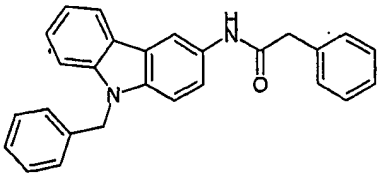
Example 29-2	2-Dimethylamino-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
Example 29-3	2-Methoxy-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
Example 29-4	*N*-(9-Methyl-9*H*-carbazol-3-yl)-succinamic acid	
Example 29-5	*N*-(9-Methyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	
Example 29-6	*N*-(9-Methyl-9*H*-carbazol-3-yl)-isobutyramide	
Example 29-7	2,2-Dimethyl-*N*-(9-methyl-9*H*-carbazol-3-yl)-propionamide	
Example 29-8	Cyclohexanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
Example 29-9	Cyclopropanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
Example 29-10	*N*-(9-Methyl-9*H*-carbazol-3-yl)-iso-nicotinamide	

Table 5b: Experimental data of the compounds listed in table 5a

	1H NMR (300MHz)		Mass Spectrum		
	solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 29-1	-		300,3633	301.6	299.2

Example 29-2	-		281,3605	282.3	-
Example 29-3	-		268,3181	269.6	-
Example 29-4	-		296,3287	297.4	295.3
Example 29-5	-		314,3904	315.1	312.6
Example 29-6	-		266,3458	267.6	366.6
Example 29-7	-		280,3729	281.5	
Example 29-8	-		306,4111	307.4	305.4
Example 29-9	$CDCl_3$	0.78 (m, 2H); 1.06 (q, 2H); 1.47 (q, 1H); 3.73 (s, 3H); 7.07-7.48 (m, 5H); 7.96 (d, 1H); 8.26 (s, 1H)	264,3299	265.5	-
Example 29-10	-		301,3509	302.6	300.0

Table 6a: Examples for compounds of general formula 30

No.	Chemical name	Chemical formula
Example 30-1	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-benzamide	
Example 30-2	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-dimethylamino-acetamide	
Example 30-3	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-methoxy-acetamide	
Example 30-4	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-succinamic acid	
Example 30-5	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	

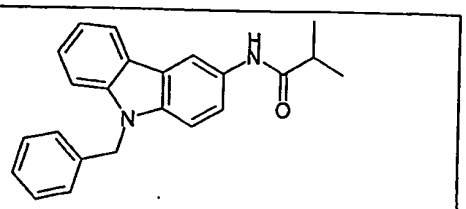
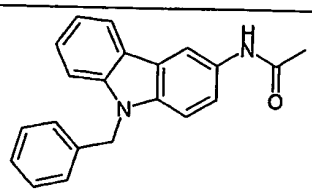
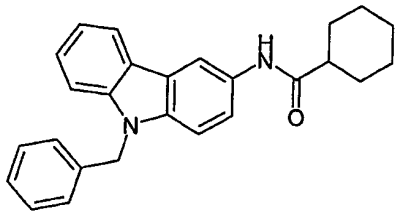
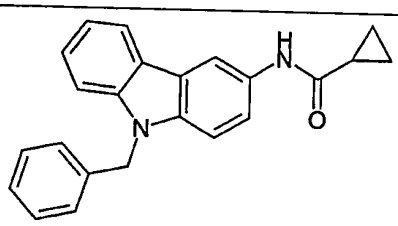
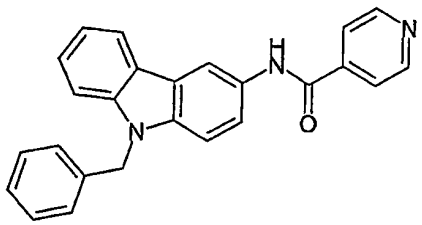
Example 30-6	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isobutyramide	
Example 30-7	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-acetamide	
Example 30-8	Cyclohexanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
Example 30-9	Cyclopropanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
Example 30-10	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isonicotinamide	

Table 6b: Experimental data of the compounds listed in table 6a

	1H NMR (300MHz)		Mass Spectrum		
	solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 30-1	-		376,4621	377.4	375.2
Example 30-2	-		357,4593	358.3	-
Example 30-3	$CDCl_3$	3.53 (s, 3H); 4.09 (s, 2H); 5.51 (s, 2H); 7.08-7.55 (m, 10H); 8.11 (d, 1H); 8.40 (m, 2H)	344,4169	345.3	343.4
Example 30-4	-		372,4275	373.0	371.2
Example 30-5	-		390,4892	391.8	388.8
Example 30-6	-		342,4446	343.3	-
Example 30-7	-		314,3904	315.0	-
Example 30-8	-		382,5099	383.3	382.0
Example 30-9	-		340,4287	341.2	-
Example 30-10	-		377,4497	378.3	376.1

Table 7a: Examples for compounds of general formula 31

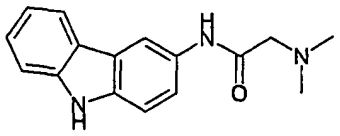
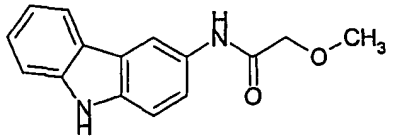
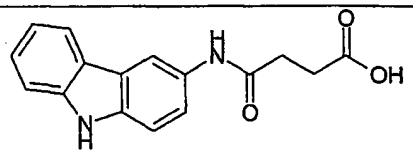
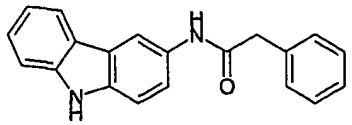
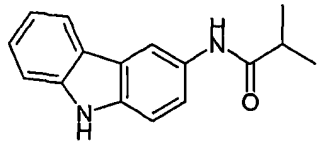
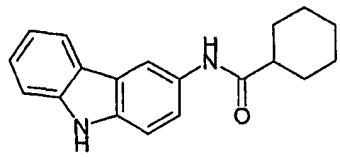
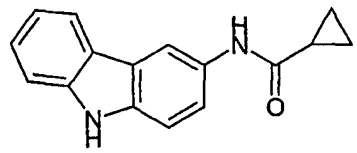
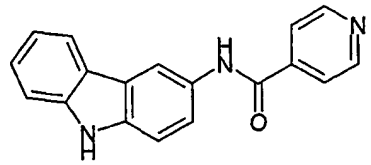
No.	Chemical name	Chemical formula
Example 31-1	*N*-(9*H*-Carbazol-3-yl)-2-dimethyl-amino-acetamide	
Example 31-2	*N*-(9*H*-Carbazol-3-yl)-2-methoxy-acetamide	
Example 31-3	*N*-(9*H*-Carbazol-3-yl)-succinamic acid	
Example 31-4	*N*-(9*H*-Carbazol-3-yl)-2-phenyl-acetamide	
Example 31-5	*N*-(9*H*-Carbazol-3-yl)-isobutyramide	
Example 31-6	Cyclohexanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
Example 31-7	Cyclopropanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
Example 31-8	*N*-(9*H*-Carbazol-3-yl)-isonicotin-amide	

Table 7b: Experimental data of the compounds listed in table 7a

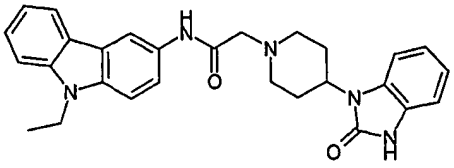
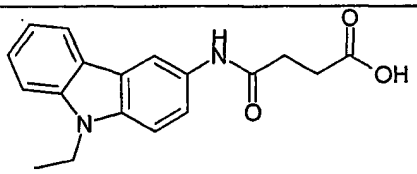
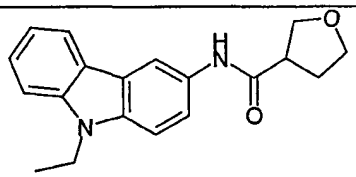
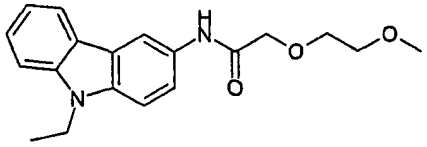
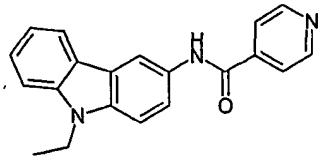
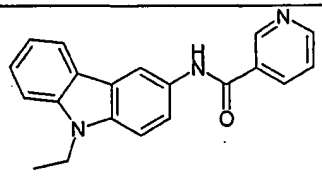
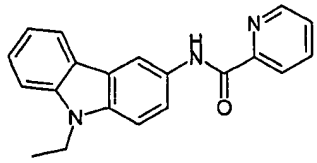
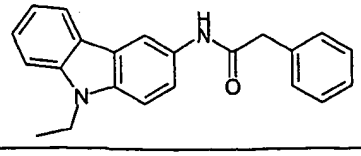
	1H NMR (300MHz)		Mass Spectrum		
	solvent	signals	calculated	$(M+H)^+$	$(M-H)^+$
Example 31-1	DMSO-d_6	2.28 (s, 6H); 3.08 (s, 2H); 7.10 (t, 1H); 7.30-7.46 (m, 3H); 7.56 (dd, 1H); 8.00 (d, 1H); 9.65 (s, 1H); 11.14 (s, 1H)	267,3334	268.5	266.3

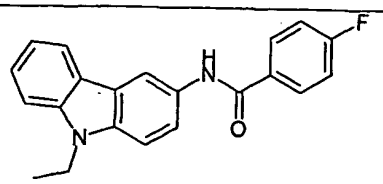
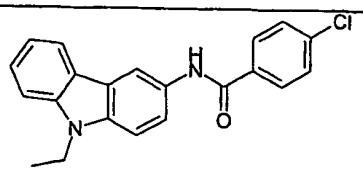
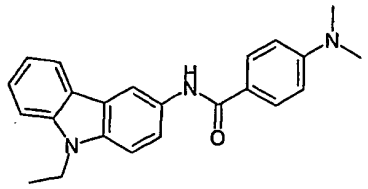
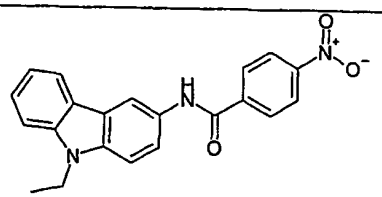
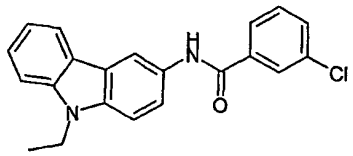
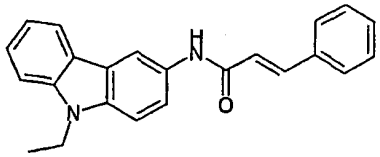
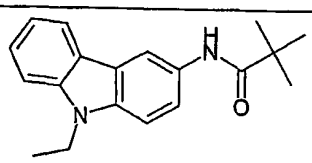
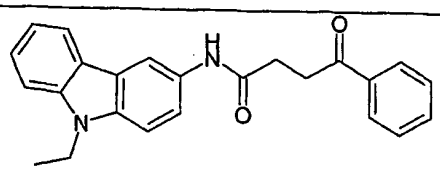
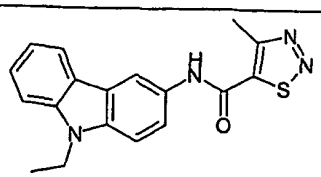
Example 31-2	DMSO-d_6	3.40(s, 3H); 4.00 (s, 2H); 7.11 (t, 1H); 7.30-7.50 (m, 3H); 7.56 (dd, 1H); 8.00 (d, 1H); 8.37 (s, 1H); 9.69 (s, 1H); 11.16 (s, 1H)	254,291	255.4	253.3
Example 31-3	-		282,3016	283.6	281.2
Example 31-4	-		300,3633	301.4	299.2
Example 31-5	-		252,3187	253.4	251.0
Example 31-6	-		292,3841	293.6	291.1
Example 31-7	-		250,3028	251.3	249.2
Example 31-8	-		287,3238	288.3	285.9

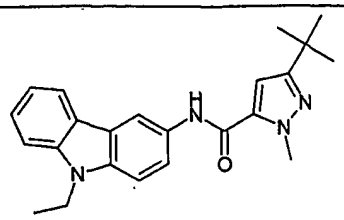
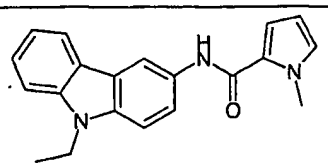
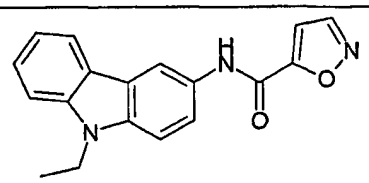
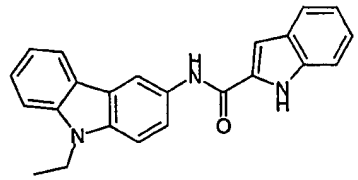
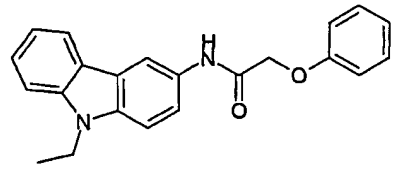
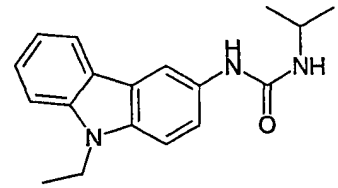
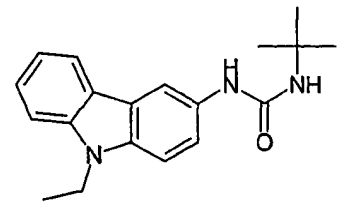
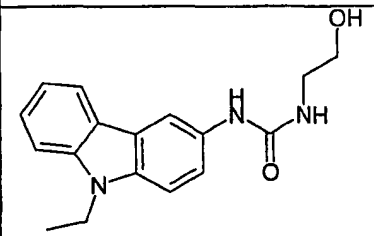
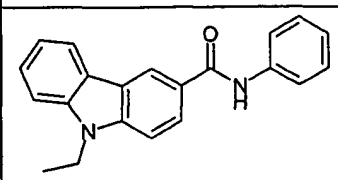
Claims

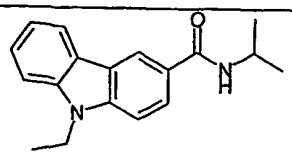
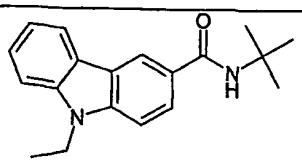
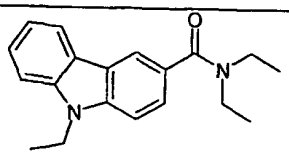
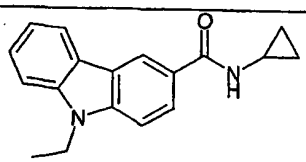
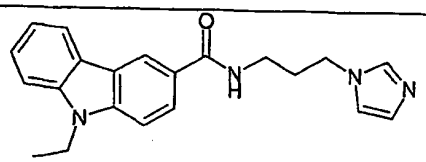
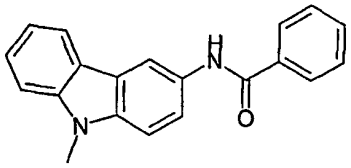
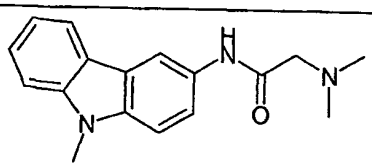
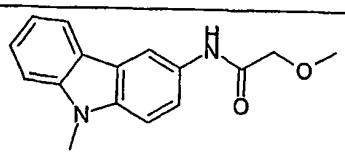
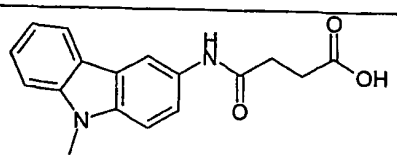
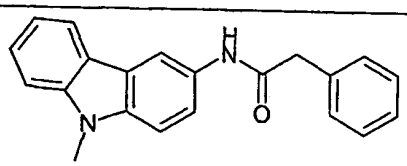
1. A compound selected from table 1:

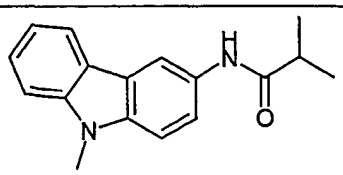
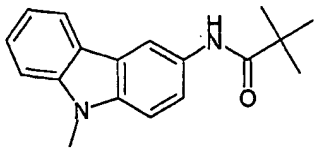
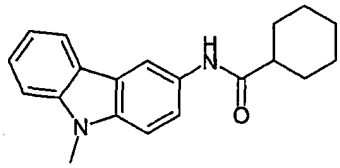
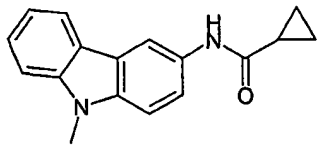
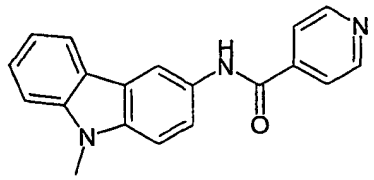
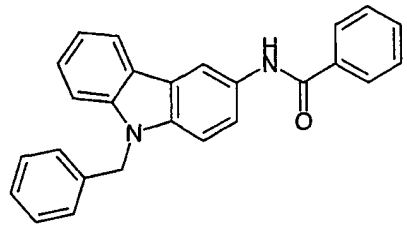
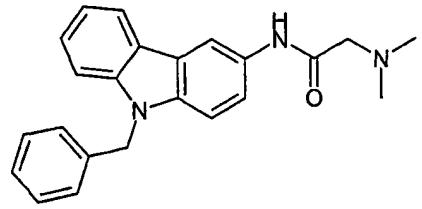
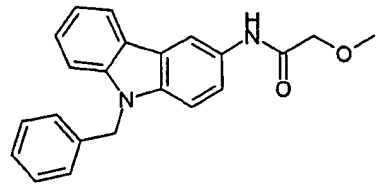
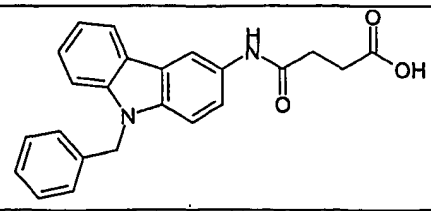
Table1:

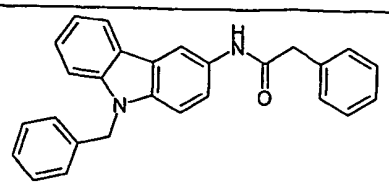
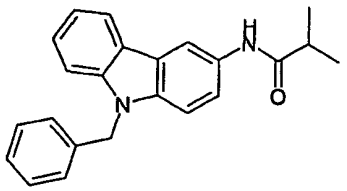
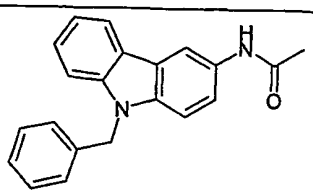
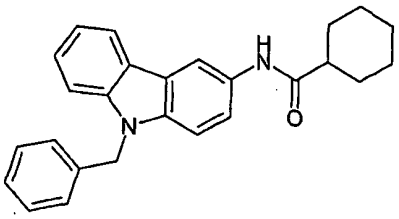
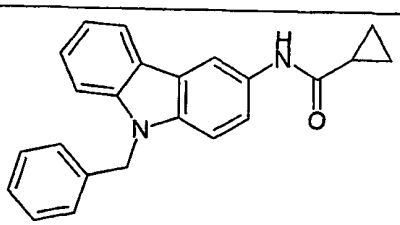
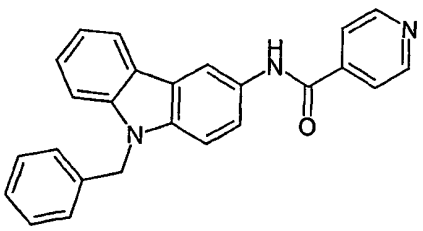
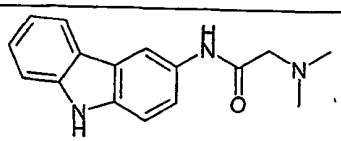
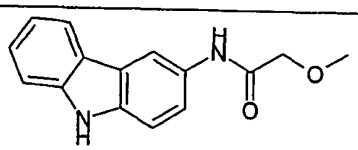
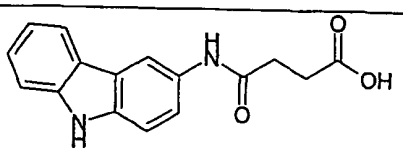
No.	Chemical name	Chemical formula
26-1	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	
26-2	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-succinamic acid	
26-3	Tetrahydro-furan-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-4	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-(2-methoxy-ethoxy)-acetamide	
26-5	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-isonicotin-amide	
26-6	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-nicotinamide	
26-7	Pyridine-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-8	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	

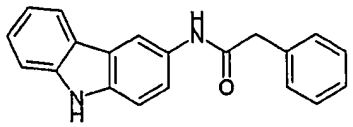
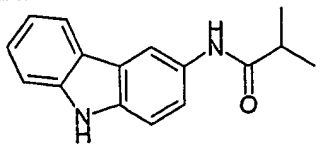
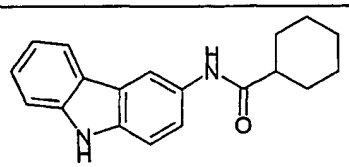
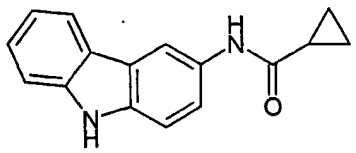
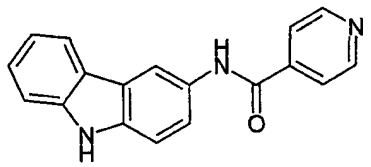
26-9	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-fluoro-benzamide	
26-10	4-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-12	4-Dimethylamino-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-13	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-nitro-benzamide	
26-14	3-Chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide	
26-15	(E)-*N*-(9-Ethyl-9*H*-carbazol-3-yl)-3-phenyl-acrylamide	
26-16	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2,2-dimethyl-propionamide	
26-17	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-4-oxo-4-phenyl-butyramide	
26-19	4-Methyl-[1,2,3]thiadiazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	

26-20	5-*tert*-Butyl-2-methyl-2*H*-pyrazole-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-21	1-Methyl-1*H*-pyrrole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-22	Isoxazole-5-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-24	1*H*-Indole-2-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide	
26-25	*N*-(9-Ethyl-9*H*-carbazol-3-yl)-2-phenoxy-acetamide	
27-1	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-isopropyl-urea	
27-2	1-*tert*-Butyl-3-(9-ethyl-9*H*-carbazol-3-yl)-urea	
27-3	1-(9-Ethyl-9*H*-carbazol-3-yl)-3-(2-hydroxy-ethyl)-urea	
28-1	9-Ethyl-9*H*-carbazole-3-carboxylic acid phenylamide	

28-2	9-Ethyl-9*H*-carbazole-3-carboxylic acid iso-propylamide	
28-3	9-Ethyl-9*H*-carbazole-3-carboxylic acid *tert*-butylamide	
28-4	9-Ethyl-9*H*-carbazole-3-carboxylic acid di-ethylamide	
28-5	9-Ethyl-9*H*-carbazole-3-carboxylic acid cyclopropylamide	
28-6	9-Ethyl-9*H*-carbazole-3-carboxylic acid (3-imidazol-1-yl-propyl)-amide	
29-1	*N*-(9-Methyl-9*H*-carbazol-3-yl)-benzamide	
29-2	2-Dimethylamino-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
29-3	2-Methoxy-*N*-(9-methyl-9*H*-carbazol-3-yl)-acetamide	
29-4	*N*-(9-Methyl-9*H*-carbazol-3-yl)-succinamic acid	
29-5	*N*-(9-Methyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	

29-6	*N*-(9-Methyl-9*H*-carbazol-3-yl)-isobutyramide	
29-7	2,2-Dimethyl-*N*-(9-methyl-9*H*-carbazol-3-yl)-propionamide	
29-8	Cyclohexanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
29-9	Cyclopropanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide	
29-10	*N*-(9-Methyl-9*H*-carbazol-3-yl)-isonicotin-amide	
30-1	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-benzamide	
30-2	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-dimethylamino-acetamide	
30-3	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-methoxy-acetamide	
30-4	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-succinamic acid	

30-5	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide	
30-6	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isobutyr-amide	
30-7	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-acetamide	
30-8	Cyclohexanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
30-9	Cyclopropanecarboxylic acid (9-benzyl-9*H*-carbazol-3-yl)-amide	
30-10	*N*-(9-Benzyl-9*H*-carbazol-3-yl)-isonicotin-amide	
31-1	*N*-(9*H*-Carbazol-3-yl)-2-dimethylamino-acetamide	
31-2	*N*-(9*H*-Carbazol-3-yl)-2-methoxy-acetamide	
31-3	*N*-(9*H*-Carbazol-3-yl)-succinamic acid	

31-4	*N*-(9*H*-Carbazol-3-yl)-2-phenyl-acetamide	
31-5	*N*-(9*H*-Carbazol-3-yl)- isobutyramide	
31-6	Cyclohexanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
31-7	Cyclopropanecarboxylic acid (9*H*-carbazol-3-yl)-amide	
31-8	*N*-(9*H*-Carbazol-3-yl)-isonicotinamide	

and the diastereomers, enantiomers, mixtures and salts thereof, particularly the pharmaceutically acceptable salts thereof.

2. A compound according to claim 1 selected from the group consisting of

(a) tetrahydro-furan-3-carboxylic acid (9-ethyl-9*H*-carbazol-3-yl)-amide
(b) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2-(2-methoxy-ethoxy)-acetamide
(c) *N*-(9-ethyl-9*H*-carbazol-3-yl)-nicotinamide
(d) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2-phenyl-acetamide
(e) *N*-(9-ethyl-9*H*-carbazol-3-yl)-2,2-dimethyl-propionamide
(f) *N*-(9-ethyl-9*H*-carbazol-3-yl)-4-oxo-4-phenyl-butyramide
(g) 2-chloro-*N*-(9-ethyl-9*H*-carbazol-3-yl)-benzamide
(h) 1-(9-ethyl-9*H*-carbazol-3-yl)-3-isopropyl-urea
(i) 1-(9-ethyl-9*H*-carbazol-3-yl)-3-(2-hydroxy-ethyl)-urea
(j) *N*-(9-methyl-9*H*-carbazol-3-yl)-isobutyramide
(k) 2,2-dimethyl-*N*-(9-methyl-9*H*-carbazol-3-yl)-propionamide
(l) cyclopropanecarboxylic acid (9-methyl-9*H*-carbazol-3-yl)-amide

and the diastereomers, enantiomers, mixtures and salts thereof, particularly the pharmaceutically acceptable salts thereof.

3. The pharmaceutically acceptable salts of a compound containing a basic group or a carboxy group according to one of the claims 1 and 2.

4. A pharmaceutical composition containing a compound according to one of the claims 1 or 2 or a salt, particularly a physiologically acceptable salt, thereof according to claim 3.

5. Process for preparing a pharmaceutical composition according to claim 4, characterized in that a compound according to at least one of claims 1 or 2 or a salt according to claim 3 is incorporated in one or more inert carriers and/or diluents by a non-chemical method.

6. Use of a compound according to one of the claims 1 and 2 or a pharmaceutically acceptable salt according to claim 3 for manufacture of a medicament for the treatment of eating and metabolic disorders.

7. Use of a compound according to one of the claims 1 and 2 or a pharmaceutically acceptable salt according to claim 3 for manufacture of a medicament for the treatment of sleep disturbance, of morphine withdrawal symptoms or of epileptic seizures.

8. Method of treating eating and metabolic disorders which comprises administering to a patient in need of such treatment a therapeutically effective amount of a compound according to one of claims 1 and 2.

9. Method of treating sleep disturbance, morphine withdrawal symptoms or epileptic seizures.which comprises administering to a patient in need of such treatment a therapeutically effective amount of a compound according to one of claims 1 and 2.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ 02/05750

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D401/14 C07D209/88 C07D405/12 C07D401/12 C07D417/12
C07D403/12 C07D413/12 A61K31/403 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BEILSTEIN Data, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 1 184 373 A (MEIJI SEIKA KAISHA) 6 March 2002 (2002-03-06) examples claim 1	1-9
X	& WO 00 63171 A 26 October 2000 (2000-10-26) ---	
X	WO 01 07409 A (DONALD SAMUEL CRAIG ;FOOTE KEVIN (GB); SCHOFIELD PAUL (GB); ASTRAZ) 1 February 2001 (2001-02-01) examples claim 1 ---	1-9
E	US 6 399 631 B1 (ELLIOTT RICHARD L ET AL) 4 June 2002 (2002-06-04) claim 2 --- -/--	1-9

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2002	09.08

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, C

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ 02/05750

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN 279979 XP002207783 abstract & LINDEMANN: CHEM. BER., vol. 57, 1924, page 557 ---	1
X	DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN 248691, 3756378 XP002207784 abstract & NOVELLI: AN. FARM. BIOQUIM., vol. 22, 1955, pages 28-32, Buenos Aires ---	1,3
P,X	DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN 8918759 XP002207785 abstract & DEADY ET AL.: "Lithiation of pivaloylamino derivatives of dibenzofuran and 9-methylcarbazole" AUST. J. CHEM., vol. 54, no. 3, 2001, page 177-180 -----	1,2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/[redacted]02/05750

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
EP 1184373	A	06-03-2002	AU	3840000 A	02-11-2000
			EP	1184373 A1	06-03-2002
			WO	0063171 A1	26-10-2000
WO 0107409	A	01-02-2001	AU	6000900 A	13-02-2001
			WO	0107409 A1	01-02-2001
US 6399631	B1	04-06-2002	NONE		

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/05750

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 8,9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1-9 (part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1 (part), 2, 3-9 (part)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-9 (part)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). The way the claims are structured (i.e. directed to single compounds rather than to a generic formula) makes it impossible to limit the structural search in any non-arbitrary way. Furthermore, as the claimed compounds are already known to have the claimed biological activity, a meaningful search cannot be carried out based on the structure linked to the activity. For this reason the documents cited in the search report constitute a non-exhaustive list of relevant prior art.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 (part), 2, 3-9 (part)

   Carbazole compounds possessing a -NHCO- group attached at the 3-position of the ring system via the N atom, their pharmaceutical compositions and uses.

2. Claims: 1 (part), 3-9 (part)

   Carbazole compounds possessing a -CONH- group attached at the 3-position of the ring system via the C atom, their pharmaceutical compositions and uses.